REMARKS

I. Status

Claims 1-7 and 12-16 were pending. Claims 1-7 were under consideration, claims 12-16 having been withdrawn from consideration. In this amendment new claims 17-26 are added. Upon entry, claims 1-7 and 17-26 will be under consideration.

The claim amendments and new claims are supported in the specification and Original claims. Support for new claims 23-26 is replete in the specification (*e.g.*, at the paragraph bridging pages 9 and 10).

II. Interview

Applicants thank Examiner Kerr for the courtesy of a telephonic interview on July 27, 2004, with the undersigned and Dr. Gary Ashley. The participants discussed the written description requirement.

III. Objections to the Specification

The specification was objected to because in the table on page 8, "ACP" was in the wrong column. The specification has been amended to correct this typographical error.

IV. Response

A. Allowable Claims

Claims 6 and 7 were objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 6 and 7 have been so amended. Accordingly, Applicants understand these claims are allowable.

New claims 17 and 18 have been added and recite the language of claims 6 and 7 prior to amendment.

B. Claims 1-5 and 17-18

The remaining issue is the rejection of claims 1-5 under 35 U.S.C. § 112, first paragraph, for alleged lack of written description. Applicants thank the examiner for her helpful comments during

the telephonic interview. Applicants also note that the case law concerning the written description requirement has become increasingly complex in recent years. However, in view of the arguments below, Applicants urge the office to reconsider the rejection of claims 1-5 and 17-18. (In addition and independently, Applicants submit that new claims 19-26 are in compliance with the written description requirement and allowable for the reasons discussed below in Sections C and D).

With regard to claims 1-5 and 17-18:

- Applicants respectfully **continue** to assert that the rejection articulated by the Office, is directed to operativeness and not to written description. In the most recent Office Action, the Office repeats, as basis for the rejection, the assertion that "still only a single species of the inhibitors is demonstrated." Applicants submit that the written description requirement does not require "demonstration." The requirement requires *description*.

- Although the Office states that only a single species is "demonstrated" Applicants submit that claims 6 and 7, which are deemed allowed once rewritten as independent claims, recite *seven* inhibitors. Accordingly, whatever deficiencies the specification allegedly may or may not have, Applicants find the assertion by the Office that only a *single* species is in compliance with Section 112 confusing. Applicants respectfully urge the Office to reconsider the instant rejection.

- Applicants reiterate the arguments made in the previous response (filed February 12, 2004).

C. Allowability of New Claims 19-22

New claims 19-22 are directed to a method for producing a desoxyepothilone, which method comprises fermentation of *S. cellulosum* in the presence of a reversible inhibitor of a P450 enzyme, where the inhibitor reduces activity of the *epo*K gene product (EpoK) as measured in an assay measuring conversion of epothilone D to epothilone B. Inhibitors of P450 are well known and several commercially available inhibitors are described in the specification (see, *e.g.*, page 10, lines 1-11). An assay for inhibition of EpoK is described at, e.g., page 20, first full paragraph.

Applicants respectfully submit, in view of the well known nature of P450 inhibitors, the nature of the target, the guidance provided by the specification, and the knowledge of one of ordinary skill in the art, a sufficient number of inhibitors is disclosed to adequately describe the claimed invention.[1]

In its rejection, the Office relies on *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997) and *Enzo Biochem* 63 USPQ2d 1609 (CAFC 2002). Both are inapposite to the instant case because the claim terms at issue (e.g., "P450 inhibitor" and "*epoK* gene product inhibitor") are not new or unknown biological materials that ordinarily skilled artisans would easily miscomprehend. See, *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 65 USPQ2d 1385 (CAFC 2003) in which the CAFC stated explained "Both *Eli Lilly* and *Enzo Biochem* are inapposite to this case because the claim terms at issue here are not new or unknown biological materials that ordinarily skilled artisans would easily miscomprehend." In *Amgen v. Hoechst* a description of protein expression in two cell types (CHO cells and COS1 cells) was deemed to adequately support claims reciting the genus "vertebrate cells" and the genus "mammalian cells."

In the present case Applicants respectfully submit that an adequate number of species are disclosed to describe the genus of reversible inhibitors of P450 enzymes that reduce activity of the *epo*K gene product as measured in an assay measuring conversion of epothilone D to epothilone B are clearly described. Seven such inhibitors are recited in claims deemed allowable by the Office and *the specification teaches that other inhibitors of P450 also inhibit the epoK gene product.* The ordinarily skilled reader of the instant application would perceive that Applicants had "possession" of the claimed invention: As discussed in Applicant's response filed February 12, 2004, P450 enzymes are characterized by a conserved structure and a common enzymatic mechanism. Individual P450 inhibitors can inhibit multiple different P450 enzymes, and individual P450 enzymes can be inhibited by multiple different inhibitors. As previously explained in the response filed February 12, 2004, the ordinarily skilled reader is aware there is a common mechanistic rationale for examining general P450 inhibitors against the P450 oxidase homolog EpoK.

Applicants submit the specification describes a representative number of species of P450 inhibitors that reduce activity of the *epo*K gene product as measured in an assay measuring

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[1] Applicants do not believe the description of the instant specification is limited to the seven inhibitors acknowledged by the Office; Applicants do assert that *even if* the disclosure was limited to the seven inhibitors such description would be adequate to support the claimed methods.

conversion of epothilone D to epothilone B and that claims 19-22 clearly comply with the Section 112 first paragraph requirements.

D. Allowability of New Claims 23-26

New claims 23-26 are directed to a method for producing a desoxyepothilone, which method comprises fermentation of *S. cellulosum* in the presence of a reversible inhibitor of a P450 enzyme. It is beyond dispute that P450 inhibitors are very well known to those of ordinary skill in the art, and that numerous examples are described in the instant specification; Applicants believe it is similarly beyond dispute that claims 23-26, which recite use of a P450 inhibitor, comply with 35 U.S.C. 112, 1st paragraph. Applicants acknowledge that it is expected that not every reversible P450 inhibitor is effective in the claimed method. However, it is *well established* that patentability does not require operability of each and every embodiment encompassed by the claim. Rather, a claim complies with the requirements of Sections 101 and 112, first paragraph, if one of ordinary skill in the art can practice the invention without undue experimentation.[2] A requirement for some experimentation does not indicate a lack enablement. Enablement simply requires that the necessary experimentation not be undue. *In re Wands*, 858 F.2d at 736-737. In the instant case, determination that a reversible P450 inhibitor is also a EpoK inhibitor (and thus suitable in the claimed method) requires only routine experimentation using, for example, an assay such as that described in detail in the instant specification (e.g., at page 20, lines 14-28). It is generally recognized that the relative skill of those in the chemical and biological arts is high, such that the provision of an assay for EpoK inhibition allows the skilled artisan to practice the claimed invention without undue experimentation.

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[2] See, for example, *In re Angstadt and Griffin* 190 USPQ 214 (CCPA 1976). In that case the Court observed:

"Appellants have apparently not disclosed every catalyst which will work; they have apparently not disclosed every catalyst which will not work. The question, then, is whether in an unpredictable art, section 112 requires disclosure of a test with every species covered by a claim. To require such a complete disclosure would apparently necessitate a patent application or applications with "thousands" of examples or the disclosure of "thousands" of catalysts along with information as to whether each exhibits catalytic behavior resulting in the production of hydroperoxides. More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid "literal" infringement of such claims by merely finding another analogous catalyst complex which could be used in "forming hydroperoxides."

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

Dated: September 23, 2004

Respectfully submitted,

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